The Enigma of the Acquired Immunodeficiency Sydnrome

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Abstract *— Investigative probes into the immunopathogenesis of the acquired immunodeficiency syndrome (AIDS) have now isolated a retrovirus known as HTLV III/LAV or Human Immunodeficiency Virus (HIV). However, in spite of this advance, the spectrum of clinical manifestations and case numbers continues to rise in conjunction with global spread. Although dental surgeons face a number of infectious diseases in their discipline including Hepatitis B, the emergence of the AIDS virus with attendant dramatic coverage by the media tends to emphasize the more fatal aspects and reinforces the point that there is neither a current drug with potential nor a vaccine on the horizon. Against this background, the article endeavours to put the disease into perspective with some diagnostic pointers and precautions during dental treatment. Infiltration of AIDS into Southeast Asia is inevitable but some insight of the implications and precautions should ensure the unimpeded treatment of patients.*

Introduction

The appearance of unusual infections linked with an impairment of the cellular immune response mechanism in homosexual men emerged as a recognised entity in the United States of America in 1981. Once some clinical and laboratory guidelines had been established it became evident that earlier cases had occurred in 1978, a finding reciprocated by investigations in Haiti. The presence of the syndrome in various forms in Central Africa, especially in Zaire and Chad, supports the postulation that the initial reservoir is located there — a point reinforced by further reports of cases in adjacent regions including Cameroun, Gabon, Kenya, Mali, Rwanda, Burundi and uganda where it is known locally as 'SLIM' disease.

Current reports through the World Health Organisation (WHO) put the number of cases over 20,000 and still rising. With the gathering momentum of the disease, the implications are widening and realisation of the extent is dawning since, in addition to the homosexual and bisexual communities, there are further groups termed as 'high risk' such as intravenous drug abusers who share needles and syringes; infants born to infected mothers (many of whom also have Hepatitis B); and sexual contacts of bisexual males and intravenous drug abusers (needle sharing). Outwith these particular groups, however, are large numbers of haemophilic patients and recipients of contaminated whole blood open to risk.

The Acquired Immunodeficiency Syndrome (AIDS) is a specific clinical entity with a wide range of infections and growths within it (Staquet *et at* 1986); has an internationally accepted definition and is known to stem from a retrovirus. Other clinical states closely linked and regarded as part of the result of the AIDS virus infection have been described and include Persistent Generalised Lymphadenopathy (PGL) and AIDS-Related Complex (ARC) — both of which may or may not eventually progress and mainfest as AIDS.

Admittedly, neither AIDS nor its related states may at present form a real threat to health in Southeast Asia. Nevertheless, if the African and North American outbreaks of the disease or, for that matter the European and Australian, are regarded as ''spread'' or ''parallel developments'', the problem remains uncontained by the population movement over the globe. The frightening aspect of the high mortality rate in AIDS is not placated by the thought that there is as yet no effective treatment for the immune defect or a vaccine although many promising strategies are being formulated Weber, 1986).

Definition

The acquired immunodeficiency syndrome (AIDS) has primarily been defined by the Centres for Disease Control (CDC) in America as the presence of a reliably diagnosed disease that is at least moderately indicative of an underlying defect in cell-mediated immunity.

Prior to examining the specific details related to AIDS it should be noted that cellular immunodeficiency disorders are reflected by some specific clinical characteristics and that in most instances, patients with partial or absolute defects in T lymphocyte cell function tend to have infections often fairly severe and untreatable.

The role of T-cells requires a little explanatory comment. It must be emphasised they mediate both effector and regulatory functions and that these distinct actions are undertaken by separate T-cell subpopulations. The main T-cell 'effector' functions are the destruction of antigen-carrying target cells by means of specific 'killer' T-cells and the formation of potent mediators. Such mediators are responsible are responsible for induction of a number of inflammatory reactions such as the chemotaxis of granulocytes and monocytes and the delayed-type hypersensitivity linked with macrophage activation.

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In the regulatory role T-cells produce *interleukin*-2 (IL-2) which is a T-cell growth factor needed to develop the cytotoxic T-cell responses. They have other influences as helper T-cells and with the collaboration of B-cells produce antibodies to thymus-dependent antibodies. Helper T-cells are also involved in structuring the class and idiotype of antibody arising in an immune response. A further set of regulatory T-cells known as the suppressor T-cells curtails and inhibits antibody synthesis, cell-mediated immune responses and the delayed type of hypersensitivity.

Defects in T-cell function manifest clinically in six major forms along with a number of other states. The form (Buckley, 1985) are consistent with the following:

1. Recurrent infections linked with low grade or opportunistic agents such as viruses, fungi or *Pneumocystis carinii*.
2. A slow cutaneous energy.
3. Presence of growth retardation, curtailed life-span, wasting and diarrhoea.
4. Susceptible to graft-versus-host disease when supplied fresh blood, plasma or unmatched allogeneic bone marrow.
5. A high incidence of malignancy.
6. Mortality from live virus or BCG vaccination.

Although any specific definition of AIDS will obviously incorporate the clinical manifestations arising from general defects in T-cell function, the disease is not represented by a single group but ranges from asymptomatic viral carriers to states described as AIDS prodrome or pre-AIDS, AIDS-related complex (ARC) and persistent lymphadenopathy syndrome (PLS). All these subsidiaries can culminate in the disease complex designated as AIDS. When no specific laboratory tests were available the tendency was to arrange the clinical manifestations to support such tests on immunodeficiency disease as were available. Such is the spectrum of the disease that even though tests on the viral antibody are now available a considerable number of the clinical criteria remain.

Definitions on AIDS and related states are reaching a new form of refinement and are aimed at providing guide-lines for hospitals, clinics and laboratories. Other classifications such as 'oral lesions' are simply a spin-off of the major disease problem and are therefore formulated more within the speciality for the speciality allowing for some degree of overlapping.

Prior to outlining the definitions applicable to AIDS and related states, it must be pointed out that such definitions only hold with the state of current knowledge and are subject to changes. The present definitions have already been modified in the light of recent research and clinical practice.

Acquired Immunodeficiency Sydrome (AIDS)

Acceptance that a case manifests AIDS means that the patient has:

(i) A reliably diagnosed disease that is at least moderately indicative of an underlying cellular immune deficiency (for example Kaposi's sarcoma in a patient aged less than 60 years or a serious opportunistic infection) who at the same time has also had:

(ii) No known underlying cause of cellular immune deficiency nor any other cause of reduced resistence reported to be associated with that disease.

A. Protozoal and helminthic infections

1. Cryptosporidiosis, intestinal, causing diarrhoea for over one month (confirmed on histology or stool microscopy).
2. *Pneumocystis carinii* pneumonia (based on histology or on microscopy of a ''touch'' preparation or bronchial washings).
3. Strongyloidosis, causing pneumonia, CNS infection or disseminated infection (on histology).
4. Toxoplasmosis, causing pneumonia or CNS infection (on histology, microscopy of a ''touch'' preparation or serology).

B. Fungal infections

1. Aspergillosis, causing CNS or disseminating infection (on culture or histology).
2. Candidiasis causing oesophagitis (on histology, microscopy of a ''wet'' preparation from the oesophagus, or endoscopic findings of white plaques on an erythematous mucosal base).
3. Cryptococcus causing plumonary, CNS, or disseminated infection (on culture, antigen detection, histology, or India ink preparation of CSF).

C. Bacterial infections

1. ''Atypical'' mycobacteriosis (species other than tuberculosis or lepra), causing disseminated infection (on culture).

D. Viral infections

1. Cytomegalvirus, causing pulmonary, gasterointestinal tract or CNS infection (On histology, culture or serology).
2. Herpes simplex virus, causing chronic mucocutaneous infection with ulcers persisting more than one month or pulmonary, gastrointestinal tract, or disseminated infection (on culture, histology, or cytology).

Progressive multifocal leukoencephalopathy (thought to be caused by papovavirus) (on histology or E.M.).

With the advent of the recent AIDS serological tests (for the HTLV III/LAV (HIV) antibody), the above definition has now been extended to include the following states:

(a) In the absence of the opportunistic diseases required above, any of the following diseases can be considered indicative of AIDS if the patient presents with a *positive* serological test for HTLV III/LAV (HIV):

1. Disseminated histoplasmosis (not confined to lungs or lymph nodes) diagnosed by culture, histology or antigen detection.
2. Isoporiasis, causing chronic diarrhoea (over one month) diagnosed by histology or stool microscopy.
3. Bronchial or pulmonary candidiasis, diagnosed by microscopy or by characteristic white plaques grossly on bronchial mucosa (not by culture alone).
4. Non-Hodgkin's lymphoma of a high-grade pathologic type (diffuse, undifferentiated) and of B-cell or unknown immunologic phenotype, diagnosed by biopsy.
5. Histologically confirmed Kaposi's sarcoma in patients who are 60 years old or older when originally diagnosed.

(b) In the absence of the opportunistic diseases as previously defined, a histologically confirmed diagnosis of chronic lymphoid interstitial pneumonitis in a child (under 13 years) can be considered indicative of AIDS unless test(s) for HTLV III/LAV (HIV) are negative.

(c) Patients with a lymphoreticular malignancy diagnosed more than 3 months after the diagnosis of an opportunistic disease used as a marker for AIDS will be included as AIDS cases.

(d) To increase the specificity of the case definition, patients will be excluded as AIDS cases if they have a negative result on testing for serum antibody to HTLV III/LAV (HIV), have no other type of HTLV III/LAV (HIV) test with a positive result, and do not have a low number of T-helper lymphocytes or a low ratio of T-helper to T-suppressor lymphocytes. In the absence of test results, patients satisfying all other criteria as per the definition will continue to be included.

Persistent Generalised Lymphadenopathy (PGL)

This title is used to cover a number of proposed AIDS related states such as Pre-AIDS syndrome, AIDS-related complex (ARC) or extended lymphadenopathy syndrome) and is defined as:

1. Lymphadenopathy at 2 or more non-inguinal sites for 3 months or longer.
2. In addition at least one of the following:
   Weight loss, fever, diarrhoea, fatigue/malaise, night sweats.
3. Plus at lest two of the following:
   Decreased ratio of T-helper: T-suppressor lymphocytes
   Decreased number of T-helper cells
   Increased serum globulin levels
   Anaemia or leukopaenia or thrombocytopaenia or lymphopaenia
   Decreased blastogenic response of lymphocytes to mitogens
   Cutaneous anergy or multiple skin-test antigens
   Increased levels of circulating immune complexes.

Aetiology

Arising from the plethora of suggested origins, current investigations appear to confirm that the acquired immune deficiency syndrome (AIDS) is linked with infection by a retrovirus known as Lymphadenopathy-Associated Virus (LAV) (Barre-Sinoussi *et al*, 1983) or Human T-Lymphotrophic Virus, Type III (HTLV III) (Gallo *et al*, 1984). Subsequently, these parallel investigations are now known to have isolated the same retrovirus which is now termed HTLV III/LAV or Human Immunodeficiency Virus (HIV). (For simplicity it will be referred to as the AIDS virus in the text). As Morgan (1986) points out, the virus belongs to a subfamily, Lentivirinae, of which only three other species are known and it is postulated that the virus may have crossed the species barrier and have been transmitted to humans more than 12 years ago (Seale, 1985).

This virus infests peripheral T-lymphocytes, specifically the ''helper'' or ''inducer'' subset — cells expressing the T4 antigen. Once this has occurred, the T-helper lymphocytes lose their functional capacity and tend to die prematurely thus leading to a steady depletion of the cellular immune system which characterises AIDS. In addition to the blood cell involvement the virus may persistently infect cells of the central nervous system (CNS), possibly the microglial cells (Weber, 1986). In the brain cells the virus is slowly replicative and can be found by the presence of an enzyme — reverse transcriptase — which differentiates it from other RNA viruses (Hoffman *et al*, 1985). Further, the virus has been observed in a cell free state in saliva (Groopman *et al*, 1984), from mononuclear cells in semen (Zagury *et al*, 1984), cerebrospinal fluid (Levy *et al*, 1985), tears (Fujikawa *et al*, 1985), breast milk (Thiry *et al*, 1985) and plasma (Wendel *et al*, 1985). Recently the AIDS virus has been isolated from the cervical secretions in women (Vogt *et al*, 1986, Wofsy *et al*, 1986). Obviously the depth of penetration of this virus into the various tissues is much greater than previously envisaged.

In simplistic terms, the retrovirus interacts initially with the cell receptor and eventually enters the cell by endocytosis. Once within the cell, the retroviral enzyme reverse transcriptase activates and sheds its coat. Subsequently, the proviral DNA can then integrate into the genetic material of the cell. Basically, the transcription of intergrated viral DNA enables the synthesis of viral proteins which amalgamate into new viruses. These new viruses migrate from the cell as mature viral particles by process of budding (Weber, 1986).

The virus, as an entity, can be inactivated by heating at 56 degrees centigrade for 30 minutes (Spire *et al*, 1985) but be viable following 48 hours at 30 degrees centigrade (Barre-Sinoussi, *et al*, 1983). Viral destruction can be attained by treating with glutaraldehyde 2% or a hypochlorite solution of 10,000 ppm.

Transmission

The original nucleus of the disease stemmed from homosexual and bisexual men, particularly in Europe and North America. However, this has been extended into the heterosexual population in these continents and was present much earlier in Africa where AIDS is distributed more evenly between males and females.

Emergence of the disease is directly related to intimate sexual contact of the homosexual type which results in the transfer of virally infected semen, infected rectal cells, blood or other body fluids. Although the homosexual/bisexual groups manifest the largest numbers of AIDS sufferers, the finding of a heterosexual element suggests that a greater spread must be expected. There are no doubts that the initial finds point to a viral transmission based on the frequency of contact with prostitutes and to the number of sexual partners (de Perre *et al*, 1985).

In addition, there are a number of other 'high risk' groups such as female sexual partners of AIDS patients, infected females passing it to children, intravenous drug abusers, and certain types of patients who have administrations of blood or blood products including plasma.

Confirmation of AIDS virus in semen (Zagury *et al*, 1984, Stewart *et al* 1985) raises problems in the western practice of Artificial Insemination by Donor (AID). Donors of semen are now screened but it is regarded that possible damage to the mucosa of the uterus during the insemination may have given access to the virus. Of other body fluids, tears (Fujikawa *et al*, 1985) and human breast milk (Thiry *et al*, 1985) may contain the AIDS virus although confirmation of transmission is uncertain. The presence of AIDS virus in the cervical secretions in women who were also seropositive for the virus (Vogt *et al*, 1986), Wofsy *et al*, 1986) is the basis of a possible heterosexual extention of the disease. AIDS virus has been reported in a cell-free state in saliva (Groopman, *et al*, 1984) but some doubts have emerged following a more recent work (Hodd *et al*, 1985) where only 1 of 83 samples derived from AIDS antibody-positive patients was confirmed. At the present time there is insufficient evidence to implicate saliva as a transmitter of the AIDS virus (Scully *et al*, 1986).

Intravenous drug abusers constitute another group directly related to the passage of the AIDS virus. In this instance, blood is transmitted by the sharing of needles and syringes between homosexual carriers of the virus and heterosexual contacts. It has been noted by Morgan (1986) that a 'chain linkage' could occur with women addicts becoming infected, then passing on the virus to male (sexual) contacts who, in turn infect other female contacts (sexually).

Investigations into the phenomenon known as ''Needle-stick or cut'' is a natural sequence to methods of drug induction used by drug addicts — to which can be added mucous membrane exposure. Such parenteral involvements to hospital staff have been reported (Wormser *et al*, 1984; Gerberding *et al*, 1985; Grint and McEnvoy, 1985; Hirsch *et al*, 1985) but in spite of extensive monitoring of all the personnel with apparent viral exposure there is no significant evidence that the disease is readily transmitted (Smithies, 1986). In fact, only one nursing staff member is known to have formedan AIDS virus antibody following such as injury (Anon, 1984).

The consensus of opinion is that the risk of transmission of the AIDS virus by needle-stick injuries or mucous membrane contact appears low, while carriers have lower viral titres than frank AIDS victims. A strict regime of observation and testing is continuing on all staff involved with AIDS patients but no seroconversion has manifested from needle-stick incidents.

Transmission does not seem to occur through casual contact or the aerosol path. Evidence supports the conjecture that the risk of AIDS virus infection following such injuries outlined above is lower than the comparable risk of transmission of Hepatitis B after a similar injury.

In general terms although the AIDS virus has been identified in various body fluids such as semen, tears, blood, breast milk and saliva, the main method of ingress into the body is through sexual intercourse or through the transfusion of blood or blood products. With this in mind, the possibility of infection should also be related to sputum, faeces, vomit, urine and pus *if* contaminatd with blood. On the other hand, current work appears to rule out infection through droplets arising from coughing or sneezing, feeding utensils, shared washing or use of articles normally used in toilet facilities.

For those involved with saliva, isolation of the AIDS virus has not proved to be a frequent occurrence and certainly it has not been implicated in kissing. If an operator is in contact with a great deal of saliva, it is more likely that contamination would arise from the presence of blood in the saliva derived from surgical and dental procedures in the mouth. The passge of the virus by means of cuts, scratches, burns can be linked with the conjunctiva or abrasions in other mucous membranes — all are possible but so far unproven.

The haematological-aided entry of the AIDS virus is of importance since persons at risk are all those involved with either blood transfusions or blood products. Comment has already been made on the possibility of percutaneous inoculation of infected blood by a contaminated needle (needle-stick), a sharp instrument or broken glass.

In the early days of AIDS recognition, transfusions and use of blood and blood products contaminated a number of patients such as haemophiliacs. In fact, Europeans and Americans were exposed to the virus for at least 4 years due to imported commercial concentrates. For perspective, there are approximately 5,000 haemophiliacs in the U.K. of which 2,000 use Factor VIII in blood plasma. Some 44% of these have antibodies to the AIDS virus (Connor, 1986). Blood plasma containing Factor VIII can be sterilised by heating for 24 hours at 68 degrees centigrade without impairing Factor VIII. From October 1985, all donated blood has been tested for the AIDS antibody.

There are two accepted methods of clearing AIDS virus from Factor VIII. Firstly, the blood plasma can be freeze-dried and then heated in its ''water-free'' state. Secondly, the Factor VIII can be suspended in an organic solvent and then heated as a ''wet sludge''. The length of time and the temperature involved varies among the various laboratories who prepare Factor VIII. However, it is known that the protein envelope encapsulating the virus is not thought to be strong enough to withstand high temperatures for long hours.

Laboratory Detection

Ingress of the AIDS virus into the body tissues is followed by an incubation period — the length of which remains open to some conjecture. The incubation period between initial infection and the production of AIDS antibodies can be longer than a year and one report (Andreani *et al*, 1983) puts it at four or more.

In homosexuals incubation ranges between 9 to 22 months (Wormser *et al*, 1983) while others regard it as occurring within 6 months in most cases and 1 to 2 months often. The short incubation period appears especially significant in children (Aman *et al*, 1983); Oleske *et al*, 1983). The sequence of incubation usually leads to an early state — a type of AIDS-related complex or prodromal illness — before some patients develop frank AIDS. Symptoms do not manifest in all patients following infection and may become ''carriers'' while others may exhibit a ''glandular fever'' kind of syndrome.

In laboratory tests, the selective diminution of the T4 lymphocyte subset in an otherwise healthy person is suggestive of an underlying immune defect. However, caution should be exercised since the reversal of the T4-T8 ratio of lymphocyte subsets does not mean that the person is at risk to frank AIDS as there are a number of both common and benign viral infections which can increase the T8 subset without relatively lowering the T4 subset — yet this may induce an inversion of the T4-T8 ratio (Fauci, 1985).

Laboratory advances have now introduced antibody tests for the AIDS virus. The antibody can be detected by means of an enzyme-linked immunosorbent assay (ELISA) or by the more sensitive electrophoretic 'Western blot' assay technique. There is, however, a considerable variance in the reported prevalence of antibody (Sallahuddin *et al*, 1984; Hirshch *et al*, 1985) because as few as 55% of positives may be demonstrated by ELISA. Another highly reliable method for testing the AIDS virus antibodies is the radio immune precipitin assay (RIPA).

Infection linked to AIDS virus can produce an antibody response and many seroconvert around the 6-12 week period. The authenticity of the presence of AIDS antibody can be clouded since both false-positive and false-negative results can emerge (Weiss *et al*, 1983; Scully *et al*, 1986). For example, patients are known to be infected with the AIDS virus but have no antibody response to its presence while with the advance and extension of the syndrome others appear to lose their AIDS antibody (Shchipbach *et al*, 1984; Mayer *et al*, 1986). In simplistic terms, if an AIDS viral antibody is detected then the patient is categorically presumed to have been infected with the virus. In addition, it could imply a carrier status but it cannot be inferred that immunity exists (Wong-Staal and Gallo, 1985). Logically, the reverse of this situation means that the absence of AIDS antibody does not award a 'carte blanche' that the virus does not exist. The present AIDS antibody test has a priority task in the screening of blood and tissue donors or women in high-risk groups possibly considering pregnancy.

Diagnosis of AIDS is a multifactorial exercise involving the wide spectrum of clinical features, the AIDS antibody tests and the immunological aspects suggestive of a severe immune defect which are demonstrated by lymphopenia linked with a marked reduction of T4 lymphocytes. The reduction of T4 lymphocytes causes a fall in the ratio of the T4-helper cells to the T8-suppressor cells. The T4-T8 ratio falls from normal acceptable of 2 to approximately 0.5 in AIDS infected persons (Shroff *et al*, 1983; Amman *et al*, 1983; Seligmann *et al*, 1984; Bowen *et al*, 1985). These findings are also pertinent to patients with the AIDS-related complex and in persons lacking in symptoms but members of high-risk groups (Jeffries, 1985).

General Patho-Symptology

Infection by the AIDS virus produces a wide spectrum of clinical manifestations ranging from the asymptomatic person to those with frank AIDS. As can be seen from the definition of AIDS previously outlined circumstances are a pointer of AIDS. For example, Kaposi's sarcoma and *Pneumocystis carinii* can manifest either together or alone in AIDS.

Setting aside the testing for AIDS antibody response or identified cause of a cellular immune defect, the implication of other diseases such as the recurrent type linked with low grade or 'opportunistic' agents — viruses, fungi, bacteria and parasitic organisms in fact reflect the sequence of events which would be expected with T-cell functional defects. One possible differing aspect may be the severity of attack and spread and manifestation at perhaps an unusual time e.g. hairy leukoplakia or a less obvious angular cheilitis — in a patient with full dentition.

As expected with such a wide range of manifestations, patients in the early phases may complain of vague symptoms such as enlarged lymph glands, fever, weight loss and perhaps night sweats. In more advanced states, pneuomocystis carinii pneumonia stemming from a protozoan organism may be present. This may be abrupt and fullminant or insidious. Cytomegaloviros infections produce a fever and are disseminated throughout the organs. The alimentary tract may be implicated with oral or oesophageal candidiasis. *Cryptococcus neoformans* infections emerge in connection with disseminated disease or meningitis. Some 24% of patients suffering with AIDS have the unusual and disseminating Kaposi's sacroma. Herpes simplex virus can become a fulminant and possible fatal mucocutaneous dissemination as also does *Mycobacterium avium-intracellulare*, a disease rarely seen but common in AIDS patients. Infection with the coccidial protozoa *Cryptosporium* shows an intractable diarrhoea.

Basically, because these types of patients have severe immunosuppression they are open to a whole range of infections and it is not uncommon that an AIDS patient may have more than one opportunistic infection at the same time. Many patients have intractable diarrhoea for which no agent can be identified. In addition the large numbers of infections and symptoms there is now evidence that nearly half the

patients may develop at some stage brain disease, schizophrenia or dementia (Mattock and Parker, 1985).

Patients who are antibody positive and eventually manifest with a fully developed AIDS remains uncertain and may be about 10% of the total (Smithies, 1986).

Finally, it must be emphasised that the lists of diseases including neoplasms, opportunistic infections, neurological states are still in a state of flux. A central, smaller group has been accepted while the greater and more peripherally placed diseases or disease-effects depend on time and an in-depth study. Many of these peripheral observations can lead to a diagnosis even if only in terms of a ''suspect case'' but cannot yet be applied as a definitive judgement without the involvement of further investigation. In the paramedical field relative to dentistry a fairly comprehensive list of conditions linked to AIDS has been recently published (Scully *et al*, 1986) and will no doubt require augmentation at a later date.

Orofacial Patho-Symptology

Since the disease process is no respecter of the boundaries between structures and tissues, manifestations of infections relative to AIDS can involve the oral cavity, facial and neck regions, separately or in combination.

Prior to examining the specific problems, it should be stressed that all the diseases listed in current literature as occurring in the oro-facial region are opportunistic, may have a common history of occurrence in the body as a whole but present themselves as a major or lesser entity in the head. It is noticable that a number of infections and tissue responses merit only one prior observation but this sparsity of sightings does not preclude that they are not significant or that further new responses may yet emerge.

Candidiasis (Candidosis): This global opportunistic mycosis is one of the few organisms which has a major manifestation in the oral region relative to AIDS. Candidiasis is a term used to denote a number of local and systemic processes with a common denominator in the colonisation or infection by the *Candida* species. The common agent is *Candida albicans* along with other species-C tropicalis; C. Krusei; C parapsilosis; C. parakrusei, C. stellatoidea; C. pseudotropicalis and C. guilliermmondi (Drutz, 1985). The fact that this microorganism is a common denizen of the mouth, the gratrointestinal tract and vagina of unaffected persons indicates that presence alone does not mean infection. Cutaneous infection usually involves trauma to the skin, maceration and continual moisture whereas systemic infection stems from severely ill patients, antibiotic-traeted patients with defects in the mucocutaneous defences. Systemic infections may be focal and confined to a body cavity i.e., the peritoneum or to the cerebrospinal fluid (CSF) or perhaps confined to the lower urinary tract. Where blood stream spread develops there may occur a self-limiting benign or progressive course. In both the cutaneous and the systemic types there are generally accepted predisposing factors such as infancy, pregnancy and old age together with the 'shielding' or 'occlusion' of the epithelial surfaces by either dressings or dentures. Thus any presence of T-cell function defects whether by primary or secondary origins will ensure some form of candidiasis. In Malaysia, as in any other tropical region, the pattern of Candida infections differs somewhat from those in temperate regions. Part of these differences stem from trends of medical therapy and in the prevalence of types of underlying disease such as diabetes mellitus. The threat of acquired immunodeficiency syndrome (AIDS) emerging in Southeast Asia remains real while the pattern of candidiasis may show a slight shift in emphasis although the major manifestations will probably be unaltered. Incidence, however, may show a perceptible rise relative to candiodiasis since the saphophytic transfer has a record of high incidence under tropical conditions.

The oral cavity in patients with a defective cell-mediated immune mechanism such as AIDS or the rare syndrome of chronic mucocutaneous candidiasis, manifests candidosis (thrush) often complemented by an oesophageal candidosis (Tavitian *et al*, 1986). The mucocutaneous infection or thrush is characterised by the grey to cream-like pseudomembrane, which can be patchy or confluent, and emerges over the tongue, buccal mucosa and related surfaces. Both ulceration and necrosis may manifest. Eventually removal of the membrane results in a red, oozing base. the pseudomembrane or plaque are formed of interlocking masses of fungal hypae interspersed with desquamated epithelial cells, keratin, fibrin, leucocytes, necrotic debris and bacteria.

Since oesophagitis is often a sequal to the oropharyngeal infection, signs or retrosternal pain and dysphagia may appear.

Oral candidosis is regarded as a common manifestation of AIDS virus and is begining to be ranked as one of the initial manifestations (Scully *et al*, 1983, 1986; Abemayor and Calcaterra, 1983; Rosenberg *et al*, 1984; Porter *et al*, 1984; Klein *et al*, 1984; Marcusen and Sooy, 1985; Bahjews *et al*, 1985; Wofford and Miller, 1985). Apart from an expected oesphageal outbreak, the presence of thrush can also highlight the liability of the patient to systemic opportunistic infections (Murray *et al*. 1985). The development of an oral candidosis may only be suggestive of an AIDS virus connection if all local causes including antibiotic treatment, corticosteroids, xerostomia with checks on blood dyscrasias have been eliminated.

Hairy Leukoplakia (Condyloma planus): The emergence of the term 'hairy leukoplakia' as a possible stable and consistent indicator of AIDS and AIDS-related diseases originated from the description of a white patch with peripheral striae on the tongues of homosexual males (Greenspan *et al*, 1984, 1985). This finding was specifically linked to papillomavirus and a herpes virus in homosexual males. Another report from the Centers for Disease Control (CDC, 1985a) postulated that the presence of a hairy leukoplakia was the forerunner of a possible characteristic AIDS. While it is fully accepted that homosexuals fall within the high-risk AIDS group, it must be remembered that infection with herpes virus (herpes simplex and varicella

zoster), *Candida*, cytomegalovirus, Epstein-Barr virus and hepatitis B virus are detectable in homosexuals with or without AIDS (Richards, 1985).

Recently hairy leukoplakia was implicated with the Epstein-Barr virus (Greenspan *et al*, 1985) but there are some doubts arising since the virus is found in normal tissue from healthy patients (Young *et al*, 1986). The clinical appearance of hairy leukoplakia is not at variance since it seems to be found in patients infected with AIDS virus and presents with white broad plaques with a predeliction for the lateral border of the tongue and a minor representation on the ventral tongue mucosa. These areas are firmly adhered and many are bordered by a circumferential straited fringe.

Although implication of hairy leukoplakia with AIDS is not questioned in the sense that the lesion is visible in an AIDS patient, its origins remain unresolved.

The recent introduction of the term ''Condyloma planus'' as a replacement for ''hairy leukoplakia'' (Eversole *et al*, 1986) is possibly another step towards clarity although the reasons for the change are still debatable. Work conducted on cervical biopsy specimens demonstrated some peculiar epithelial cell changes described as 'hollowing' and were named as 'koilocytes' and the phenomenon as 'koilocytotic atypia (Koss and Durfee, 1956). This kind of change was observed as visible white lesions in the loweer female reproductive tract. They could be demonstrated by the use of dilute acetic acid hence their name of aceto-white lesions (Meisels and Fortin, 1976; Meisel *et al*, Reid *et al*, 1980; Reid *et al*, 1982, Reid *et al*, 1984). Types 6 and II human papillomavirus have been linked with these aceto-white lesions and further work showed virion arrays in the nuclei of koilocytes (Dunn and Ogilive, 1968; Torre *et al*, 1978; Hills and Laverty, 1979; Morin and Meisels, 1980). As Eversole *et al*, (1986) points out, the aceto-white lesions actually represent flat or planar condylomas. The microscopic features arising from an investigation of hair leukoplakia in homosexual men appears to have a close resemblance to structures in the papillomavirus-linked flat condylomas of the lower female and male genital tacts. Evidence of human papillomavirus relative to hairy leukoplakia is so far inconclusive so that the full usage of the term ''condyloma planus'' awaits the results of current investigations.

Kaposi's sarcoma: A rare neoplasm of multifocal origin, Kaposi's sarcoma or multiple idiopathic haemorrhagic sarcoma, manifests as red-purple to dark brown plaques, nodules and macules of the skin and other organs. In the skin the initial appearance may be of annular, serpiginous and blue-red patches (Schwartz *et al*, 1980). Later some ulceration may appear in the plaques and nodules. Localisation to one area is known (cox *et al*, 1970) or it remains as a single lesion with no signs of progression (Cox and Helwig, 1959). The lesions may extend to the subcutaneous lymph nodes with enlargement (Amazon and Rywlin, 1979) and visceral involvement such as the gastrointestinal tract, lungs, liver, abdominal lymph nodes and heart (Tedeschi *et al*, 1947; Tedeschi, 1958; Cox and Helwig, 1959; Anthony and Koneman, 1960; Temime *et al*, 1961; Staquet *et al*, 1986). In the dermal type, lymphatic blockage is common with an ensuing elephantiasis while the disease is slow with nodules involuting producing atrophic scarring and pigmentation. Elsewhere, visceral lesions are only found in 10% of patients who may died from haemorrhage, intercurrent infection, visceral extension or complicating malignant lymphomas.

The disease is found in Mediterranean peoples and African negroes and the dermal form which may last from 1-25 years (average 5-10 years), is associated with the Mediterranean group and specifically older men with lesions often on the lower extremities with lymphatic blockage. Although the latter group was first described in 1872, it was only in 1950 that a high incidence of Kaposi's sarcoma manifested in tropical Africa with an epicentre in central and eastern Zaire and Western Uganda (Hutt and Siegler, 1984). The African disease occurs among the young and men of middle age but with a greater visceral involvement in addition to the cutaneous manifestations. Identification of at least four clinical types has been made including the nodular skin lesions which are multifocal and small with patients having a benign course and normal length of life; the florid skin lesions which are fast growing, often fungating and may penetrate to deep tissues and bone; the infiltrative skin lesions which implicate the deeper skin structures and form clinically observable indurated and oedamatous plaques; and finally, the lymphadenopathic type which s particularly common in children, rapidly spreads into many organs and manifests conjunctival and mucosal nodules. Incidence for males and females in childhood is similar. There are many children who present only with the skin lesions who do not show a rapid disease progression (Slavin *et al*, 1970).

The emergence over recent years of a fatal form of Kaposi's sarcoma — similar to the African type — in young homosexual men in the United States has stimulated new interest into the disease with a range of connections to secondary primary malignancies and opportunistic infections that involve immune defects and the role of infectious and environmental factors. Kaposi's sarcoma has now become the characteristic malignant neoplasm occurring in AIDS. Such patients appear to be affected in the fourth decade and their cutaneous lesions are generalised in distribution and appear smaller, softer and less dark in colour than the classic form of firm indurated leg lesions. Mucocutaneous manifestations or even visceral or lung lesions may precede the skin lesions.

Early oral manifestation is common with the presence of a red or purple macule or nodule often on the palate (Eversole *et al*, 1983; Smith, 1984; Nickles *et al*, 1984). Both single and multiple lesions can occur on the palate and invariably above the maxillary second molar — a purple macule which may ulcerate and become haemorrhagic, usually symptomless (Farthing *et al*, 1986). A common skin lesion occurs on the tip of the nose. Cervical lymph nodes and salivary gland implication may present prior to either mucocutaneos or visceral signs. Orally, the common sequence of manifestation of macules is firstly the palate, secondly the lips followed by tongue and then later the pharyngeal wall. A number of facial skin lesions can mimic conditions such as

pyogenic granuloma, dermatofibroma and malignant melanoma. The medial third of the lower eye lid is favoured by Kaposi's lesions and a linear distribution of lesions may be observed on the neck following the skin folds (Farthing *et al*, 1986).

Kaposi's sarcoma exhibits variable histological features with a lesion possibly consisting of a perfusion of small capillary-type blood vessels or, a cellular lesion with growing masses of young spindle cells — variable in size, shape and appearance with few mitotic figures — and vascular slits. These lesions usually have an inflammatory infiltrate.

In context of Southeast Asia, given the tropical conditions, Kaposi's sarcoma is uncommon even though African-type conditions exist in places like Papua-New Guinea. However, the original spread of the now recognised AIDS by homosexuals has now been furthered by heterosexual links and the use of blood and blood products. With the spread of the acquired immune deficiency syndrome continuing the emergence of lesions of Kaposi's sarcoma are only a matter of time.

Cervical lymphadenopathy: Understandingly, with a defect in the cell-mediated immunity as found in AIDS, there is a very marked decreased in the host defences which, inevitably leads to a tremendous susceptibility to the various recurrent opportunistic infections. It has been noted that patients infected with the AIDS virus can develop a Burkitt-like lymphoma. A large number of male homosexuals have presented with an unexplained lymphadenopathy defined by the Centers for Disease Control (CDC) as the presence for three months or longer of extrainguinal sites of lymphadenopathy with no specific cause to account for it. So far, biopsies have only shown a non-specific lymphoid hyperplasia irrespective of which part of the body the specimen originated.

The existence of oral lymphomas in the presence of AIDS have been reported (Scully *et al*, 1983; Porter *et al*, 1984; Rosen, 1985; Weiss *et al*, 1983) but these are not yet a common occurrence. On the other hand, cervical lymphadenopathy appears to be a common sighting in AIDS and AIDS threatened patients (Abemayor and Calcaterra, 1983; Marcusen and Sooy, 1985; Scully *et al*, 1986).

Miscellaneous lesions: The advent of any new disease means that much information needs to be collated before the final pattern of the disease process can be approached comprehensively. Insofar as the AIDS problem is concerned, the four orofacial lesions already described are probably the most common but wide ranging observations relative to other recognisable lesions are still emerging.

Two rashes on the skin of the face have been linked to AIDS. These are Molluscum contagiosum and Seborrhoeic dermatitis. The former consists of a variable number of small, discrete, skin-coloured, dome-shaped papules, about 2-4 mm in size with a centre. When fully developed a curd-like substance can be expressed from the centre. They can be markedly inflamed. The latter shows a sharply demarcated brown-red area with a fine scaling resembling psoriasis. There may be oozing but no vesicles.

Angular cheilitis is a common dental problem but it is not usually associated with a full normal dentition. Its presence, therefore, would be suspect.

Both types of recognised herpesvirus infections (herpes simplex virus and varicella-zoster virus) have manifested in AIDS patients. The herpes simplex virus infections have been noted as severe and persistent (Rosen, 1985), but so far has not shown many signs of disseminating (Armstrong, 1984).

Veneral warts (Condyloma acuminatum) are fairly soft verrucous papules which could lead to invasive squamous cell carcinoma. In the mouth they tend to be more flattened and will not produce the cauliflower-like masses as observed on the penis, female genitals and around and in the anus (Silverman *et al*, 1986).

Recurrent ulceration is becoming more prevalent in AIDS patients. Although the classification of such ulcers occuring in the non-AIDS patient can be formulated as recurrent aphthous minor; recurrent aphthous major; recurrent herpetiform ulcerations and recurrent ulcers with Behcets syndrome, only recurrent aphthous major has been noted as associated with AIDS (Yarchoan *et al*, 1986), but the others may yet arise.

Cytomegalovirus (CMV) is one of the opportunistic diseases which takes advantage of a defect in the cell mediated immune system. It is known to replicate in epithelium as well as in fibroblastic elements. Having a global distribution it can be acquired in less well developed parts of the world at infancy, at or just after parturition. CMV infections in healthy people is usually asymptomatic although a primary infection may produce a 'glandular fever-like' manifestation. Patients undergoing open heart surgery and others receiving multiple units of blood may present with a 'glandular fever' later. In addition CMV infections present major obstacles to allograft recipients. This type of infection is now prominent in AIDS patients. Children suffering from AIDS virus have been found with a CMV parotitis (Marcusen and Sooy, 1985; Jonckheer *et al*, 1985).

Mycobacterial ulceration in the mouth of AIDS patients has been reported (Garber and Weathers, 1985). Disseminating histoplasmosis was observed in AIDS patients and oral lesions were found complementing the infection. These appeared mianly nodular but can be ulcerative and be in most areas of the mouth including the tongue, palate, lips, buccal mucosa and gingiva. Clinical appearances show ulcerations with a non-specific grey membrane and induration.

Typical epithelial squamous cell carcinoma is known to arise in certain AIDS patients (Conant *et al*, 1982; Lozada *et al*, 1982) but there is no direct evidence that the carcinoma was stimulated specifically by the AIDS infection.

With tissue resistance lowered by the AIDS infection it is

not surprising to have incidents of osteomyelitis (Pogrel, 1984), progressive periodontitis, xerostomia (Silverman *et al*, 1986). Addisonian pigmentation and sinusitis (Poole *et al*, 1984; Marcusen and Sooy, 1985). The incidence of dental abscesses in those with the AIDS virus appears to be common.

Precautionary Measures

Infectivity

The general consensus at the present time accepts that all AIDS antibody positive persons should be considered capable of transmitting the infection, and it is presumed that they will remain infected throughout life. Both European and American experience indicates that the AIDS virus is not easily transmitted to medical or paramedical staff who work with patients known to be antibody positive. In spite of this, however, because of the serious nature of the infection, logic dictates that clinical procedures of a high standard must be adhered to in order to minimise exposure to infectious material and reduce the risk of transmission (Greenspan *et al*, 1986). Standard precautions, originally formulated to combat infection from Hepatitis B appear to be highly suitable in most aspects since Hepatitis B is known to be more infective.

General Aspects

Dental practitioners should be able to safely treat persons having the positive antibody response to the AIDS virus in their normal surgeries by observing the precautions outlined. There may be situations whereby the dental surgeon may wish to establish whether a specific patient has an HTLV III/LAV (HIV) positive antibody response. The normal procedure is for the patient to be referred to their medical adviser who will examine and arrange for such a test if deemed necessary. The one proviso is that if the patient does not wish to cooperate, then they may be treated *but* on the assumption that the test is ''positive''

The clinical techniques must be of a high standard such as used to prevent transmission of any infection and is expected to be practised by *all* involved in the dental procedures and on *all* patients. Responsibility of the dental surgeon is paramount relative to protection of all their employees inclusive of dental hygienists and dental surgery assistants. Because of the close similarity in patient contact of the dentist, the dental hygienists are expected to take the same precautions during dental work on HTLV III/LAV (HIV) antibody positive patients.

Specific Precautions

Open cuts, fresh abrasions and open skin lesions should be covered with a waterproof or other suitable dressing when treating patients with known or suspected HTLV III/LAV (HIV) antibody positive response. Protective clothing such as gowns, gloves facemasks and goggles must be used by all dental personnel directly involved in dental procedures.

Disposable equipments and materials should be used when possible including napkins, mixing surfaces and mouthwash containers. Obviously, disposable needles must be used and a fresh cartridge of local anaesthetic must be used on each patient.

Instruments which are not disposable should be sterilised preferably by autoclaving. Sterilisable handpieces must be used. Non-disposable instruments should be sterilised immediately the dental procedure has terminated by placing in saturated steam in an autoclave — at 2.2 bar, 134°C maintained for a minimum of 3 minutes, or by hot air, at 160°C for 1 hour. Further disposable used instruments that cannot be incinerated or other method of destruction must be autoclaved before being discarded.

Instruments or equipment that normally cannot be dealt with by autoclaving should first be decontaminated in 2% glutaraldehyde for 1 hour. The equipment can then be physically cleaned in detergent and warm water to remove organic matter, then rinsed and left to soak in 2% glutaraldehyde for 3 hours.

When faced with external surfaces of equipment and contaminated working surfaces which are not suitable for autoclaving, cleansing must be achieved with *freshly* prepared sodium hypochlorite 10,000 ppm available chlorine (household bleach/diluted one part bleach to ten parts water) and left in contact with it at least for 30 minutes before rinsing and drying. Because hypochlorite can damage metal and fabric surfaces an alternative is a swabbing down with a solution of 2% glutaraldehyde and left in contact with it for at least 3 hours before rinsing and drying. Other external surfaces which only have a suspected contamination can be wiped with a concentration of hypochlorite (1000 ppm available chlorine) or freshly prepared 2% glutaraldehyde.

Spittoons, receivers and evacuation systems must be cleaned and flushed after each patient with a solution of 2% glutaraldehyde. After the last patient, 2% glutaraldehyde should be added to the vacuum system collector and left for a minimum of 3 hours.

Handling of contaminated equipment requires that personnel should be suitably dressed in gown and gloves and, if there is any concern and risk of splash, a mask and protective eyewear. Special care is needed if any sharp dental instruments and needles are to be handled as gloves provide no protection. Care also is needed when needles and sharps are being used for collection of specimens such as blood and tissue specimens. This undertaking must only be executed by trained and experienced staff with gloves, gowns, mouth and eye protection. Needles must be removed most carefully from syringes without resheathing them (about 40% of self-inoculation accidents occur in resheathing needles) and the fluid gently discharged into its container avoiding external contamination. If, by chance, external contamination does occur it should be redressed by disinfection. Disposable sharps should be placed immediately into a puncture-proof bin which is suitable for incineration but which must not be overfilled. Non-disposable items should be placed in a suitably secure enclosure for later disinfection

or sterilisation and finally, surface soiling at the site must be disinfected immediately.

Dental impressions should be achieved by using a silicone based material. The impressions, dentures (if there) and other appliances should then be sent to the laboratory where they should be decontaminated in 2% glutaraldehyde for 1 hour. Following this period they should be rinsed and transferred to a fresh solution of 2% glutaraldehyde and left to soak for 3 hours or, preferably, overnight if possible. The prolonged immersion will not affect the dimension stability of the impressions in a silicone based material.

Disposable materials such as napkins, contaminated gloves, disposable gowns, containers, swabs, cotton wool rolls etc. must be double bagged in plastic bags and preferably labelled witha hazard warning before incinerating according to local practice.

Disposable material (holders, swabs etc.) must be used for intra-oral X-ray film support. The dental surgeon should wear gloves and the radiographer suitably warned of the problem.

Dental personnel directly involved in dental procedures should wear a gown which can withstand a washing temperature of 90°C for 10 minutes. Non-disposable items such as gowns, white coats and towels can be safely washed in the hot wash of an ordinary washing machine. The washing temperature should be 90°C for 10 minutes. The temperature employed in the cycle is adequate to inactivate the virus, therefore decontamination of the washing machine is not necessary. In large practices or hospitals these items should be double bagged and clearly labelled according to the approved local practice for infected linen. Current methods favour the infected material in a water soluble plastic bag (either alginate stitched or Polyvinyl alcohol (PVA) and washed at the temperature designated for infected laundry — usually 93°C for 10 minutes.

Conclusion

Complacency for whatever reason in the practice of the precautions — which also provide an efficient defence against hepatitis B infection — will be superceded by disaster because the number of cases of AIDS continues to rise relentlessly in the United States, Europe, Australia, South America and Central Africa. For example, taking southern Italy for instance, the virus has spread dramatically among drug abusers. One year ago 6% of drug abusers were antibody positive, today the proportion is about 75% and spilling out of this particular group. Hence spread is inevitable although the rate of spread or its next geographic target are unknown.

Medical services can manage the medical problems that accompany and characterise AIDS to some degree of success but no particular drug currently holds great promise. Although there is a possibility of achieving virustasis by inhibiting reverse transcriptase, this in conjunction with therapy to modulate the immune system may provide some answer. On the vaccine future, in spite of forecasts it is going to be some time. Research into vaccines has just entered a new area. The use of new adjuvents, such as iscoms (Immunostimulating complexes), to present antigens in a more immunogeneic manner; new synthetic proteins sequenced genes inserted into vectors; and anti-idiotype antibodies may lead to a new preventive approach (Weber, 1986).

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